IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re application of | : | Attorney Docket No. 2005_0459A |
| Takeshi KAWAZOE et al. | : | **Confirmation No. 2807** |
| Serial No. 10/528,150 | : | Group Art Unit 1617 |
| Filed March 17, 2005 | : | Examiner Sahar Javanmard |
| EXTERNAL PREPARATION FOR INHIBITING KELOID FORMATION | : | **Mail Stop: APPEAL BRIEFS-PATENTS** |

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## APPEAL BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The following is Appellants' Brief, submitted under the provisions of 37 CFR § 41.37. Pursuant to the provisions of 37 CFR § 41.20, this brief is submitted with the required fee of $540.00.

The fee for a one month Extension of Time is also submitted herewith.

***The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975.***

## I. REAL PARTY IN INTEREST

The real party in interest is TEIKOKU SEIYAKU CO., LTD., the assignee of record, as recorded at Reel 018103 and Frame 0504.

## II. RELATED APPEALS AND INTERFERENCES

There are no related prior or pending appeals, interferences or judicial proceedings known to Appellants, Appellants' legal representative, or assignee, which may be related to, directly affect or be directly affected by, or have a bearing on the Board's decision in the pending appeal.

## III. STATUS OF CLAIMS

The status of the claims is as follows.

Claims pending: 5-7

Claims rejected: 5-7

Claims cancelled: 1-4

Claims appealed: 5-7

A complete copy of all of the pending claims is provided in the attached Claims Appendix.

## IV. STATUS OF AMENDMENTS

The claims are those set forth in the Amendment After Final Rejection, filed May 26, 2009.

The Examiner did not indicate whether the amendments submitted after final rejection would be entered, for purposes of appeal. However, in accordance with 37 CFR § 1.116(b), since the only amendment was to cancel claim 3, Appellants presume this amendment will be entered, for purposes of appeal.

## V. SUMMARY OF CLAIMED SUBJECT MATTER

A concise explanation of the subject matter defined in the independent claims involved in the appeal is presented below.

Independent claim 5 refers to a method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury which comprises administering a medicament containing acetylsalicylic acid in an effective amount to a wound lesion of a patient. Support for the claimed subject matter is found on page 2, lines 6-8; page 3, line 15 – page 4, line 1; page 4, lines 18-23; and Test 1 on pages 15-16 of Appellants' specification, filed March 17, 2005.

Independent claim 6 refers to a method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury which comprises administering a medicament containing acetylsalicylic acid in an effective amount of 0.005 to 1000 μg/g per tissue weight to a wound lesion of a patient. Support for the claimed subject matter is found on page 3, line 15 – page 4, line 1; page 4, lines 18-23; page 5, lines 11-14; and Test 1 on pages 15-16 of Appellants' specification, filed March 17, 2005.

Independent claim 7 refers to a method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury which comprises administering a medicament containing acetylsalicylic acid in an effect amount of 0.01 to 800 μg/g per tissue weight to a wound lesion of a patient. Support for the claimed subject matter is found on page 3, line 15 – page 4, line 1; page 4, lines 18-23; page 5, line 14; and Test 1 on pages 15-16 of Appellants' specification, filed March 17, 2005.

## VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 5-7 are unpatentable under 35 U.S.C § 112, first paragraph, based on the Examiner's position that the specification, while enabling for the treatment of keloid and/or hypertrophic scar formation, does not reasonably provide enablement for the inhibition/prevention of keloid and/or hypertrophic scar formation.

Whether claims 5-7 are unpatentable under 35 U.S.C. § 112, second paragraph, as being indefinite, based on the Examiner's position that it is unclear what stage of dermal or wound injury is being referred to in Appellants' statement "in a course of therapy of wound or dermal injury".

Whether claims 5-7 are anticipated under 35 U.S.C. § 102(b) based on Cappelli-Schellpfeffer (WO 01/70210).

## VII. ARGUMENT

***Rejection Under 35 U.S.C. § 112, First Paragraph***

The rejection of claims 5-7 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. [Claim 3 has been cancelled.]

The Examiner takes the position that the specification is not enabling for the inhibition/prevention of keloid and/or hypertrophic scar formation.

Appellants' claims (e.g., claim 5) recite a method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury by topically administering acetylsalicylic acid to a wound lesion of a patient.

The skilled artisan would recognize that inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury is fully enabled by the present specification, especially the results of Tests 1 to 4, more specifically the result of Test 1.

The claims of the present application relate to a method for "preventing a disease" (keloid formation, etc.), wherein aspirin is administered in a course of therapy of wound or dermal injury, namely aspirin is applied to the lesion of **open wound**, and not to the lesion or around the lesion of the healed wound.

The present invention does not claim a method for preventing keloid or hypertrophic scar formation by application of aspirin to **normal skin**, nor does it claim a method for treating or healing a keloid or hypertrophic scar **which is already formed**.

As shown in Test 1 of the present specification, the inhibition effect is confirmed while aspirin treatment is carried out **on a burn wound** for 3 weeks (not a healed wound).

Therapy of a keloid which is already formed is very difficult, and surgical treatment for it is accompanied with pain, etc. Therefore, the inhibition of formation of keloid or hypertrophic scar has been recently emphasized and evaluated by medical doctors in this field.

As discussed above, Appellants assert that the subject matter of claims 5 to 7 does not require any undue experimentation for the skilled artisan, and thus the specification is clearly enabling for the rejected claims. Accordingly, it is respectfully requested that the above rejection be withdrawn.

***Rejection Under 35 U.S.C. § 112, Second Paragraph***

The rejection of claims 5-7 under 35 U.S.C. 112, second paragraph, is respectfully traversed. [Claim 3 has been cancelled.]

The Examiner takes the position that it is not clear from Appellants' statement, "in a course of therapy of wound or dermal injury", what state of dermal or wound injury is being referred to. The Examiner further states that it is not clear if it is at the open wound stage or near the end of the scarring stage.

According to MPEP 2173.02, the definiteness of claim language must be analyzed, not in a vacuum, but in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation which would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

The phrase "in a course of therapy of wound or dermal injury" is clearly explained on page 2, lines 6-7 and 9, and page 3, lines 21 to 26 of the present specification. Test 1, on pages 15-16 of the specification, also clearly explains this language.

Specifically, the drug was applied once after the burn wound was created, and then evaluated three weeks later. Excellent effect of inhibition of the scar contracture on the burn wound after epithelization was confirmed in the group of Examples 2, 3 and 4 [containing acetylsalicylic acid for 3 weeks-treatment], comparing with the [control] group of ointment base-administration. (See page 16, lines 5 to 9.)

It is quite clear from the claim language, analyzed in light of Appellants' specification, that "in a course of therapy of wound or dermal injury" includes open wound stage, and not closed wound stage, or the stage after scar formation.

Therefore, it is respectfully requested that the above rejection be withdrawn.

***Rejection Under 35 U.S.C. § 102(b)***

The rejection of claims 5-7 under 35 U.S.C. § 102(b) as being anticipated by Cappelli-Schellpfeffer (WO 01/70210) is respectfully traversed. [Claim 3 has been cancelled.]

The present invention relates to a method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury which comprises administering a medicament containing acetylsalicylic acid in an effective amount to a wound lesion of a patient.

An object of the present invention provides a method for inhibiting keloid and/or hypertrophic scar **formation,** in a course of therapy of wound or dermal injury. This is distinct from a method for treatment of an already formed keloid or hypertrophic scar.

As discussed above, the phrase "in a course of therapy of wound or dermal injury" includes open wound stage, but does not include closed wound stage or the stage after the formation of hypertrophic scar or keloid.

The following is explained by Cappelli-Schellpfeffer (abbreviated hereafter as "C-S"): "The terms 'healed wound' or 'scar' include closed wound or a wound surface that is closed by regrowth of epithelial barrier. A wound is 'closed' after an open wound has been re-epithelialized. Closed wounds can result in the formation of a scar, ..." (See page 6, lines 16 to 19).

Therefore, it is clear that Appellants' claimed methods are not taught or suggested by C-S, because the term wound in C-S never refers to an open wound.

The Examiner takes the position that C-S specifically teaches the topical application of aspirin on the surface of a scar or healed wound, including keloids.

However, C-S does not disclose that acetylsalicylic acid is effective for treating hypertrophic scar or keloid which is already formed, or for inhibition of keloid and/or hypertrophic scar formation, with any working example. According to Example 1 of the reference, the combination of nabumetone and diphenhydramine was orally administered to a patient with hypertrophic acne scar. Hydrogel or a gel was co-administered with the drugs and topically applied as gel sheeting . . . (See page 28, lines 19-24.) According to Example 2, nabumetone was orally administered to a patient with hypertrophic tender scar. Hydrogel sheeting was topically applied . . . (See page 29, lines 16-19.) According to Example 3, nabumetone was orally administered to a patient with erythematous hypertrophic scar. Hydrogel sheeting was topically applied . . . (See page 29, last line to page 30, line 3.)

According to Example 4 of C-S, a combination of 2% salicylic acid and hydrogel was topically applied to the patient (see page 30, lines 21-23). The patient had orally received acetylsalicylic acid to prevent thromboembolic post-operative complications (scar, etc.) (See page 30, lines 15-16.) According to Example 5 of Cappelli-Schellpfeffer, a combination of 2% salicylic acid and hydrogel was topically applied to the patient (see page 31, lines 6-8).

As explained above, acetylsalicylic acid was never topically administered to the patients in order to treat a scar or a keloid. In the case of topical administration, the effect on a scar was confirmed only on 2% salicylic acid. In case of nabumetone, the effect on a scar, etc. was confirmed only when the drug was orally administered, followed by topical application of hydrogel. Surprisingly, in Example 4 of the reference, acetylsalicylic acid (325mg tablet) was already orally administered to prevent thromboembolic post operative complications, before receiving the treatment of salicylic acid.

**C-S reveals that even when acetylsalicylic acid is orally administered to the patient suffering from post-operative scar, acetylsalicylic acid is not effective and therefore, salicylic acid-treatment is further necessary.**

There is no data in C-S supporting that **topical** acetylsalicylic acid is effective for treating keloid or hypertrophic scar.

Although acetylsalicylic acid is a cyclooxygenase inhibitor, it was not confirmed that most cyclooxygenase inhibitors exhibit effectiveness for treating keloid or hypertrophic scar, and only salicylic acid exhibits such an activity in case of topical application with hydrogel.

In addition, many non-steroidal acidic anti-inflammatory drugs, which are also cyclooxygenase inhibitors, are listed in the Text Book enclosed herewith. [Also enclosed herewith is an exerpt from Wikipedia demonstrating that most NSAIDS act as cyclooxygenase inhibitors.] Of course, salicylic acid and nabumeton are listed therein. Based on the fact that only two compounds show the efficacy for treating hypertrophic scar or keloid, it cannot be said that a skilled artisan would expect that all cyclooxygenase inhibitors would show the same efficacy for hypertrophic scar or keloid.

As mentioned above, the Examiner asserts that C-S teaches a topical method, which includes administering to an individual having a healed wound or scar a therapeutically effective amount of a cyclooxygenase inhibitor directly on the surface of the scar. [It is acknowledged that acetylsalicylic acid is taught as a cyclooxygenase inhibitor.]

Although acetylsalicylic acid is a cyclooxygenase inhibitor, the Examiner must recognize that such an effect by acetylsalicylic acid is not confirmed by the reference. An opinion that (topical) acetylsalicylic acid is effective for treating hypertrophic scar or keloid would be completely based on speculation, and not based on the teachings of the reference.

Further, even if the Examiner disagrees with the above-arguments, and maintains that C-S is enabling for topical application of aspirin to treat hypertrophic scar or keloid, this method still fails to teach or suggest Appellants' claimed method. Specifically, the time (stage) for treating keloid or scar is completely different between the present invention and C-S. As explained above, according to the present invention, aspirin is topically administered while open wound and dermal injury is treated (i.e., keloid or scar is not yet formed). On the other hand, according to C-S, the drug (such as aspirin) is administered to hypertrophic scar or keloid already formed.

In Test 1 of Appellants' specification, in a heat wound model test by using type 2 diabetic modeled mice, the excellent effect of acetylsalicylic acid on prevention (inhibition) of the scar contracture on the burn wound after epithelialization is confirmed. (See Table 8.) Furthermore, in Test 2, on inhibition of collagen gel shrinking in vitro, the shrinking of collagen was inhibited in the group containing acetylsalicylic acid. (See Tables 9 and 10.) This data demonstrates that acetylsalicylic acid is effective for inhibition of the formation of a keloid or scar in a course of therapy of wound or dermal injury. Furthermore, according to Tests 3 and 4, acetylsalicylic acid does not delay the wound healing by the topical administration thereof. (See Tables 11 and 12.)

As explained above, it is shown that acetylsalicylic acid, when it is topically administered in a course of therapy of wound or dermal injury, inhibits the formation of a keloid or scar without delay of wound healing. On the contrary, Cappelli-Schellpfeffer discloses that cyclooxygenase inhibitors are administered to a healed wound or scar formed after treatment of a wound or dermal injury to improve the surface or size thereof.

Therefore, the cited reference fails to teach each and every limitation of Appellants' claims. Accordingly, it is respectfully requested that the rejection of claims 5 to 7 under 35 U.S.C. § 102(b) be withdrawn.

## ***Conclusion***

For the foregoing reasons, the invention of claims 5-7 is enabled, definite and patentable over the reference relied upon by the Examiner. Thus, reversal of the final rejection is respectfully requested.

Attached hereto are a Claims Appendix, an Evidence Appendix and a Related Proceedings Appendix.

This brief is submitted with the requisite fee of $540.00.

Respectfully submitted,

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## VIII. CLAIMS APPENDIX

**1-4. (Cancelled)**

**5. (Appealed)** A method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury which comprises administering a medicament containing acetylsalicylic acid in an effective amount to a wound lesion of a patient.

**6. (Appealed)** A method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury which comprises administering a medicament containing acetylsalicylic acid in an effective amount of 0.005 to 1000 μg/g per tissue weight to a wound lesion of a patient.

**7. (Appealed)** A method for inhibition of keloid and/or hypertrophic scar formation in a course of therapy of wound or dermal injury which comprises administering a medicament containing acetylsalicylic acid in an effect amount of 0.01 to 800 μg/g per tissue weight to a wound lesion of a patient.

## IX. EVIDENCE APPENDIX

1. Non-steroidal anti-inflammatory drug, Wikipedia
2. Pharmacology by Diseases

## X. RELATED PROCEEDINGS APPENDIX

None